

a determination of asynchrony between alleles of one or more DNA loci, which replicate synchronously in normal diploid cells, or a determination of synchrony between alleles of one or more DNA loci, which replicate asynchronously in normal diploid cells, provides positive predictability of prostate cancer in the individual.

53(New). The method of claim 52, wherein the cells are subjected to a growth stimulus before step (b).

54(New). The method of claim 52, wherein the cells are subjected to chromatin and/or DNA modifiers before step (b).

55(New). The method of claim 54, wherein the cells are subjected to chromatin and/or DNA modifiers selected from the group consisting of 5-azacytidine, Trichostatin A, Sodium Butirate, and N-nitroso-n-methylurea.

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56(New). The method of claim 52, wherein the body fluid is selected from the group consisting of blood, amniotic fluid, urine, and saliva.

57(New). The method of claim 56, further including the step of isolating cells from bodily fluids.

58(New). The method of claim 56, wherein the blood is peripheral blood.

59(New). The method of claim 58, further including the step of isolating peripheral blood cells.

60(New). The method of claim 52, wherein the cells are lymphocytes.

61(New). The method of claim 52, wherein the locus or loci are non-coding DNA regions.


62(New). The method of claim 52, wherein the locus or loci are selected from satellited DNA arrays.

63(New). The method of claim 52, wherein the locus or loci are centromere-associated.

64(New). The method of claim 52, wherein the locus or loci are tumor-associated genes.

65(New). The method of claim 52, wherein the locus or loci are selected from the group consisting of oncogenes, tumor suppressor genes, and transcription factors.

66(New). The method of claim 52, wherein the locus or loci replicate synchronously in normal diploid cells.

 67(New). The method of claim 66, wherein the locus or loci are expressed biallelically.

68(New). The method of claim 66, wherein the locus or loci are selected from the group consisting of HER2, CMYC, TP53, RB1, D21S55, D15S10, D22S75 and DSTS WI-941 and alpha, II and III satellites for all chromosomes.

69(New). The method of claim 52, wherein the locus or loci replicate asynchronously in normal diploid cells.

70(New). The method of claim 69, wherein the locus or loci are expressed monoallelically.

71(New). The method of claim 70, wherein the locus or loci are selected from the group consisting of GABRB3 and SNRPN.

72(New). The method of claim 70, wherein the locus or loci are selected from imprinted loci, loci on the X-chromosome in female individuals, and loci subjected to allelic exclusion.

73(New). The method of claim 72, wherein the imprinted locus is the Prader-Willi locus.

74(New). The method of claim 52, wherein the determination of asynchrony is a change in synchrony of replication timing of between about 3% to about 55% relative to replication timing in normal individuals.

AL 75(New). The method of claim 74, wherein the change in synchrony is an increase in asynchrony of between about 15% to about 35%.

76(New). The method of claim 74, wherein the change in synchrony is a decrease in asynchrony of about 10% to about 20%.

77(New). The method of claim 52, wherein synchrony of replication timing is determined by fluorescence *in situ* hybridization.

78(New). A method for diagnosing breast cancer, comprising:

- a) obtaining cells from a body fluid in an individual suspected to have breast cancer; and
- b) determining the synchrony between alleles of one or more DNA loci in said cells, wherein a determination of asynchrony between alleles of one or more DNA loci, which replicate synchronously in normal diploid cells, or a determination of synchrony between alleles of one or more DNA loci, which replicate asynchronously in normal diploid cells, provides positive predictability of breast cancer in the individual.

79(New). The method of claim 78, wherein the cells are subjected to a growth stimulus before step (b).

80(New). The method of claim 78, wherein the cells are subjected to chromatin and/or DNA modifiers before step (b).

81(New). The method of claim 80, wherein the cells are subjected to chromatin and/or DNA modifiers selected from the group consisting of 5-azacytidine, Trichostatin A, Sodium Butirate, and N-nitroso-n-methylurea.

82(New). The method of claim 78, wherein the body fluid is selected from the group consisting of blood, amniotic fluid, urine, and saliva.

83(New). The method of claim 82, further including the step of isolating cells from bodily fluids.

84(New). A method of claim 82, wherein the blood is peripheral blood.

85(New). The method of claim 84, further including the step of isolating peripheral blood cells.

86(New). The method of claim 78, wherein the cells are lymphocytes.

87(New). The method of claim 78, wherein the locus or loci are non-coding DNA regions.

88(New). The method of claim 78, wherein the locus or loci are selected from satellited DNA arrays.

89(New). The method of claim 78, wherein the locus or loci are centromere-associated.

90(New). The method of claim 78, wherein the locus or loci are tumor-associated genes.

91(New). The method of claim 78, wherein the locus or loci are selected from the group consisting of oncogenes, tumor suppressor genes, and transcription factors.

92(New). The method of claim 78, wherein the locus or loci replicate synchronously in normal diploid cells.

93(New). The method of claim 92, wherein the locus or loci are expressed biallelically.

94(New). The method of claim 92, wherein the locus or loci are selected from the group consisting of HER2, CMYC, TP53, RB1, D21S55, D15S10, D22S75 and DSTS WI-941 and alpha, II and III satellites for all chromosomes.

95(New). The method of claim 78, wherein the locus or loci replicate asynchronously in normal diploid cells.

96(New). The method of claim 95, wherein the locus or loci are expressed monoallelically.

97(New). The method of claim 96, wherein the locus or loci are selected from the group consisting of GABRB3 and SNRPN.

98(New). The method of claim 96, wherein the locus or loci are selected from imprinted loci, loci on the X-chromosome in female individuals, and loci subjected to allelic exclusion.

99(New). The method of claim 98, wherein the imprinted locus is the Prader-Willi locus.

100(New). The method of claim 78, wherein the determination of asynchrony is a change in synchrony of replication timing of between about 3% to about 55% relative to replication timing in normal individuals.

101(New). The method of claim 100, wherein the change in synchrony is an increase in asynchrony of between about 15% to about 35%.

102(New). The method of claim 100, wherein the change in synchrony is a decrease in asynchrony of about 10% to about 20%.

103(New). The method of claim 78, wherein synchrony of replication timing is determined by fluorescence *in situ* hybridization.

104(New). A diagnostic test for confirming prostate or breast cancer comprising:

allelic replication viewing means for viewing the pattern of behavior of at least one coding and/or noncoding;

a standardized table of replication patterns; and

analysis means for determining an altered pattern of behavior of DNA entity, whereby the altered pattern is diagnosed as a cancer characteristic.

105(New). The test according to claim 104, wherein said allelic replication viewing means is fluorescence *in situ* hybridization.


106(New). The test according to claim 104, wherein said analysis means is capable of analyzing replication patterns of the coding and/or noncoding DNA entity selected from the group consisting essentially of expressed genes and unexpressed DNA entities responsible for the segregation of genetic material.

107(New). A method of detecting agents causing genomic destabilization associated with either changes in the pattern of behavior of an allele in relation to its counterpart (allele-specific behavior) and/or losses and gains of chromosomes comprising the steps of:

applying an agent to isolated cells; and
analyzing coding and/or noncoding DNA status of the isolated cells whereby an altered pattern corresponds to genomic (genetic) destabilization.

108(New). A method for screening and identifying potential anti-cancer compounds, comprising:

contacting malignant cells having allele miscoordination with a potential anti-cancer compound;

 screening for inhibition of allele miscoordination in the malignant cells contacted with the potential anti-cancer compound; and

identifying whether or not the potential anti-cancer compound is a candidate drug for anti-cancer therapy by its ability to inhibit allele miscoordination in the malignant cells.

109(New). The method of claim 108, wherein the malignant cells are malignant T-lymphocytes.

110(New). The method of claim 108, wherein the malignant cells are renal carcinoma cells prostate cancer cells, ovarian cancer cells, or breast cancer cells.

111(New). A method for screening a candidate drug compound for carcinogenicity, comprising:

contacting non-malignant cells with a candidate drug compound;

screening for allele miscoordination; and

identifying whether or not the candidate drug compound is carcinogenic by its ability to cause allele miscoordination.

112(New). The method of claim 111, wherein the non-malignant cells are T-lymphocytes.
